METHOD FOR IDENTIFYING CANCER-SPECIFIC ANTIBODIES UTILIZING IMMUNE CHECKPOINT INHIBITION

TECHNICAL FIELD

[0001] The presently disclosed subject matter relates generally to a method for identifying cancer-specific antibodies utilizing immune checkpoint inhibition.

BACKGROUND

[0002] Immune checkpoints are a normal part of the immune system. Generally, their role is to prevent an immune response from being too strong and destroying healthy cells in the body. As part of an effort to harness a cancer patient's own immune system to fight his/her cancer, immunotherapy drugs that belong to a category of immune checkpoint inhibitors have been developed. Those drugs generally work by blocking checkpoint proteins, thus preventing an inhibition of the immune response to cancer cells. For example, administration of immune checkpoint inhibitors may allow T cells to kill cancer cells. Inhibition of immune checkpoints in cancer patients may also result in inducing the cancer patient's B cells to generate antibodies against the cancer cells.

[0003] Immune checkpoint inhibitors may be are less toxic and easier to tolerate than most chemotherapy drugs, and they are already in use with a wide range of cancer types. The present disclosure provides a method for utilizing immune checkpoint inhibitors for isolation and characterization of cancer-specific antibodies from the patient being treated.

SUMMARY

[0004] In accordance with the present invention, various embodiments of utilizing immune checkpoint inhibitors for isolation and characterization of cancer-specific antibodies and methods of generation of cancer medication/s thereof are disclosed. In one embodiment, the present disclosure provides a method for identifying cancer-specific antibodies utilizing an immune checkpoint inhibition treatment in a subject who has cancer comprising the steps of:

[0005] a. obtaining cancer cells and/or their components, and normal cells and/or their components from the subject who has cancer;

[0006] b. administering the immune checkpoint inhibition treatment to the subject who has cancer;

[0007] c. allowing time for generation of an immune reaction against the cancer cells in the subject who has cancer;

[0008] d. obtaining a serum sample from subject who has cancer, the sample comprising any antibodies which may have been generated against the cancer cells;

[0009] e. optionally discontinuing the immune checkpoint inhibition treatment of the subject who has cancer;

[0010] f. removing from the serum of step d antibodies that bind to the normal cells and/or components by incubating the serum with a cell culture prepared of the normal cells and/or their components of step a, allowing sufficient time for antibodies/antigens binding and generation of antibodies/antigen complexes, and removing and keeping the supernatant;

[0011] g. selecting the antibodies that bind to the cancer cells and/or their components by incubating the supernatant of step f with a culture of the cancer cells and/or their components of step a, allowing sufficient time for antibodies/antigens binding and generation of antibodies/antigen complexes, keeping the culture comprising antibodies/antigen complexes for further analysis and discarding the supernatant;

[0012] h. extracting the antibody/antigen complexes from the culture of step g;

[0013] i. separating the antibodies and the antigens of the antibody/antigen complexes of step h using standard protocols;

[0014] j . analyzing the antigens of step i are using standard methods for antigen identification, such as mass spectrometry; and,

[0015] k. identifying sites or regions on the antigens of step j which are specific to the cancer cells or their components obtained from the subject who has cancer in step a.

[0016] In some embodiments, the presently disclosed method comprises using the antigens of step j, or the sites or regions, identified in step k to produce a medication, wherein the medication may be antibodies specific to the antigens of step j, or sites or regions of step k, or other therapeutic agents specific to the of step j, or sites or regions of step k, or to related antigens. In some embodiments, a method of treating a subject who has cancer is disclosed, the method comprising administering to said subject a therapeutically effective amount of a pharmaceutical composition comprising the medication produced using the of step j, or sites or regions identified in step k, as described above.

[0017] In some embodiments, a method of treating a subject who has cancer is disclosed, the method comprising administering to said subject a therapeutically effective amount of the isolated antibodies of step i, wherein the antibodies are either unmodified or modified.

[0018] In some embodiments, the structure or sequence, or both, of at least one of the antigens' antibody/antigen attachment sites of the antibodies/antigens complexes of step i is determined, and the antigen's antibody/antigen attachment site is used as a treatment target for non-antibody based cancer treatments. In some embodiments, at least one of the antigen's antibody/antigen attachment sites is used as a vaccine administered to an animal for creation of antibodies specific to the antigen's antibody/antigen attachment site. In some embodiments, a method of treating a subject who has cancer is disclosed, the method comprising administering to said subject a therapeutically effective amount of the said antibodies specific to the antigen's antibody/antigen attachment site, wherein the antibodies are either unmodified or modified.

[0019] In some embodiments, a method of detecting B cells which generate antibodies against the cancer cells in the subject who has cancer is disclosed, the method comprising the steps of:

[0020] a. determining the amino acid sequence of the at least one of the antigen's antibody/antigen attachment sites and synthesizing and labeling a peptide comprising at least part of the said amino acids sequence, or labeling the at least one of the antigen's antibody/antigen attachment sites; and,